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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,617	12/11/2003	Ming-qun Xu	NEB-214-US	9524

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NEW ENGLAND BIOLABS, INC.
32 TOZER ROAD
BEVERLY, MA 01915

EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,617	XU ET AL.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 17, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *9-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-31* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9-17-04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a method of purifying, classified in class 435/183, for example.

II. Claims 9-11, drawn to a method of making an affinity matrix, classified in class 530/333, for example.

III. Claims 12-13, drawn to an affinity matrix, classified in class 435/174, for example.

IV. Claims 14-27, drawn to methods of screening ligand-binding proteins, classified in class 435/DIG 2, for example.

V. Claim 28, drawn to a method of enhancing immunogenicity, classified in class 436/823, for example.

VI. Claim 29, drawn to a fusion protein, classified in class 435/193, for example.

VII. Claim 30, drawn to a fusion protein, classified in class 424/9.34, for example.

VIII. Claim 31, drawn to a method of screening carriers, classified in class 436/517, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, II, IV, V and VIII are drawn towards various methods that are independent and patentably distinct from each other. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation and different functions. For example, Invention I is a method of purifying requiring the step of elution, which is not a required step in any other Invention. Invention II is a method of making an affinity matrix requiring the step of cleaving an intein fusion protein, which is not a required step in any other Invention. Invention IV is a method of screening proteins requiring the step of detection, which is not a required step in any other Invention. Invention V is a

method of enhancing immunogenicity requiring the step of eliciting an immune response, which is not a required step in any other Invention. Invention VIII is a method of screening carriers requiring the step of determining carrier-matrix affinity, which is not a required step in any other Invention.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product of Invention III can be used in a method of eliciting an immune response.

Inventions I and (VI or VII) are related as products and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention VI or VII can be used in a method of eliciting an immune response.

Inventions II and (III or VI or VII) are related as process of making and products made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process of Invention II can be used to make another materially different product, such as an immunogen.

Inventions III and (IV or V or VIII) are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product of Invention III can be used in a method of imaging cells or tissues.

Inventions III and (VI or VII) are independent and patentably distinct. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation because Invention III requires a matrix or a ligand-binding molecule, while Inventions VI or VII require Hha methylase or paramyosin.

Inventions IV and (VI or VII) are related as products and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention VI or VII can be used in a method of eliciting an immune response.

Inventions V and (VI or VII) are related as products and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention VI or VII can be used in a method of imaging cells or tissues.

Inventions VI and VII are independent and patentably distinct. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different modes of operation because Invention VI requires Hha methylase, while Invention VII requires paramyosin.

Inventions (VI or VII) and VIII are related as products and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as

claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products of Invention VI or VII can be used in a method of imaging cells or tissues.

Because these inventions are distinct for the reasons given above and the search required for each group is not required for the other groups, restriction for examination purposes as indicated is proper.

During a telephone conversation with Harriet Strimpel on February 1, 2005, a provisional election was made without traverse to prosecute the Invention I, claims 1-8. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because of the following informalities:

> A preliminary examination of this application reveals that the application includes terminology that is not generally accepted in the art to which this invention pertains. For example, the term "carrier" is essentially defined as a matrix-binding molecule. The specification does not provide a definition of "matrix-binding molecule" but provides a definition of "matrix" as any structure capable of immobilizing a carrier. These definitions appear to be circular. Although the specification provides examples of "matrix-binding molecules", including monosaccharide-binding domain, maltose-binding domain, vitamin binding-domain, etc., since the specification does not appear to define the term "domain," it is not clear what structure(s) constitute a "domain" or whether "domain" refers to an organic compound, or a polymer, or a polypeptide, or a specific class of protein, or a specific protein, or a specific region of a specific protein. Applicants are required to provide a clarification of these matters or correlation with art-accepted terminology so that a proper comparison with the prior art can be made. Applicant should be careful not to introduce any new matter into the disclosure (i.e., matter which is not supported by the disclosure as originally filed).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The specific claim rejections under 35 USC 112, second paragraph, set forth infra, may be considered relevant to other claims not explicitly mentioned, as deemed reasonably appropriate.

Claim 1 omits the essential step(s) of forming a carrier or a ligand with a C-terminal thioester. See MPEP § 2172.01. In addition, the recitation of "optionally" is indefinite because it is unclear whether subsequent verbiage contains required claim limitations. In addition, in step (c), the recitation of "the ligand" is indefinite because it is not clear whether "the ligand" refers to free ligand or carrier-bound ligand. Replacement of "the ligand" with "the carrier-ligand" may obviate this rejection. In addition, in step (d), the recitation of "the immobilized ligand" lacks antecedent basis and is indefinite because it is not clear how the ligand is immobilized, or what structures are involved in immobilization, or whether specific interactions are required for immobilization, or whether non-specific adsorption is required for immobilization.

In claims 1 and 3-7, the recitation of "carrier" or "matrix-binding molecule" or "matrix-binding protein" or the various chemical-binding domains listed in claim 4 is indefinite because the specification does not provide concise definitions for any of these terms. On pp. 17-18 of the specification, the term "carrier" is essentially defined as a matrix-binding molecule. The specification does not provide a definition of "matrix-binding molecule" but provides examples, including monosaccharide-binding domain, maltose-binding domain, vitamin binding-domain, etc. However, since the specification does not appear to define the term "domain," it is not clear what structure(s) constitute a "domain" or whether "domain" refers to an organic compound, or a polymer, or a polypeptide, or a specific class of protein, or a specific protein, or a specific region of a specific protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. (US 6,365,418) in view of Kent et al. (US 6,307,018).

Wagner et al. teach a method for purifying a ligand-binding molecule (see col. 12, line 9, "antibodies") from a mixture (see col. 32, lines 54-55, "complex mixture of proteins") comprising the steps of: forming a carrier-ligand conjugate (see col. 8, lines 64-66, "the affinity tag is covalently attached to the protein-capture agent... via chemical conjugation"), the carrier-ligand being immobilized on a matrix (see col. 8, line 49, "organic thinfilm"), contacting the carrier-ligand conjugate with a mixture containing the ligand-binding molecule (see col. 32, lines 54-55, "complex mixture of proteins"), selectively binding the ligand-binding molecule (see Title, "protein-capture"), and eluting the ligand-binding molecule (see col. 27, lines 33-42).

Wagner et al. do not perform a thioester-nucleophile reaction between said carrier and said ligand.

However, Kent et al. teach a method of reacting a thioester with a nucleophile for ligating peptides together to form conjugate peptides (see Fig. 1). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method for purifying ligand-binding molecules of Wagner et al. with the step of reacting a thioester with a nucleophile because Kent et al. discovered that "thioester-mediated amide-forming ligation chemistry is compatible with the use of completely unprotected peptide segments

with a full range of side chains functionalities," which results in a simple and practical approach to protein ligation (see col. 6, lines 45-53).

With respect to claim 2, Wagner et al. teach a method wherein the ligand-binding molecule is an antibody (see col. 12, line 9, "antibodies") and the mixture is an antiserum (see col. 6, line 59, "serum").

With respect to claims 3-6, Wagner et al. teach a method comprising a chitin-binding domain (see col. 23, line 44, "chitin-binding protein").

With respect to claim 7, the chitin-binding domain (see col. 23, line 44, "chitin-binding protein") of Wagner et al. necessarily teaches a chitin matrix, and would be so recognized by persons of ordinary skill in the art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
02/18/05